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COMPUTED TOMOGRAPHY-GUIDED FRAMELESS STEREOTACTIC RADIOTHERAPY FOR STAGE I NON–SMALL-CELL LUNG CANCER: A 5-YEAR EXPERIENCE

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Purpose: Stereotactic radiotherapy (SRT) is highly effective for brain metastases from non–small-cell lung cancers (NSCLCs). As such, primary lesions of NSCLC may also be treated effectively by similar focal high-dose SRT.

Methods and Materials: Between October 1994 and June 1999, 50 patients with pathologically proven T1–2N0 M0 NSCLC were treated by CT-guided frameless SRT. Of these, 21 patients were medically inoperable and the remainder were medically operable but refused surgery. In most patients, SRT was 50–60 Gy in 5–10 fractions for 1–2 weeks. Eighteen patients also received conventional radiotherapy of 40–60 Gy in 20–33 fractions before SRT.

Results: With a median follow-up period of 36 months (range 22–66), 30 patients were alive and disease free, 3 were alive with disease, 6 had died of disease, and 11 had died intercurrently. Local progression was not observed on follow-up CT scans in 47 (94%) of 50 patients. The 3-year overall survival rate was 66% in all 50 patients and 86% in the 29 medically operable patients. The 3-year cause-specific survival rate of all 50 patients was 88%. No definite adverse effects related to SRT were noted, except for 2 patients with a minor bone fracture and 6 patients with temporary pleural pain.

Conclusions: SRT is a very safe and effective treatment for Stage I NSCLC. Additional studies involving a larger patient population and longer follow-up periods are warranted to assess this new treatment for early-stage lung cancer.

CT-guided, Frameless, Stereotactic, Radiotherapy, Lung cancer.

INTRODUCTION

Stereotactic radiotherapy (SRT) and stereotactic radiosurgery have been shown to be highly effective treatments for brain metastases from non–small-cell lung cancers (NSCLCs) (1, 2). This suggests that the primary lesions of NSCLC, which are small in size, may be effectively controlled by similar focal high-dose SRT (3). In SRT of brain lesions, the radiation beams often pass through many critical neurologic pathways, and the high-dose radiation volumes are at times close to critical structures. Despite these limitations, SRT and stereotactic radiosurgery have been shown to be safe and effective treatments for brain lesions. On the other hand, in the treatment of small pulmonary lesions, the ratio of high-dose radiation volume to low-dose radiation volume should be smaller than for the brain. Moreover, limited volumes of radiation damage in the lung are not likely to cause severe adverse symptoms compared with those in the brain (3). Thus, we believed that SRT of small lesions of NSCLCs should be effective and safe. With these hypotheses and a CT-guided radiotherapy (RT) unit, we started SRT of lung cancer 7 years ago (3). In this report, our 5-year treatment results of Stage I NSCLCs are presented.

METHODS AND MATERIALS

To perform SRT for lung cancer, we developed a fusion of CT and linear accelerator (linac)(FOCAL) unit (3–6). The FOCAL unit is a combination of a linac, a CT scanner, an X-ray simulator, and a carbon table. The

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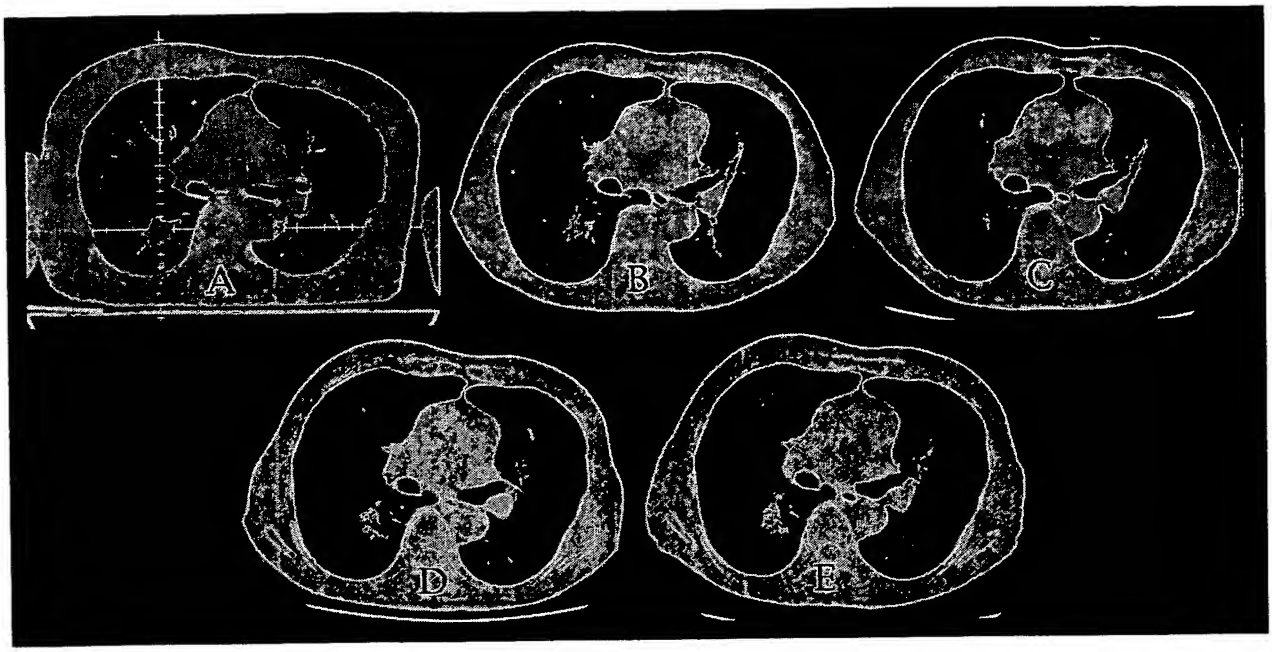

Fig. 1. T1N0 M0 adenocarcinoma of the lung. (A) A 2.5-cm tumor is seen in the center image of the positioning CT scan on the treatment day. This CT image was scanned slowly (4 s/scan) with shallow respiration. SRT of 50 Gy in 5 fractions during 1 week was given at the 80% isodose line of 3.5 cm in diameter. (B) Two months after SRT, the tumor had shrunk. (C) Fifteen months after SRT, the tumor disappeared. (D) Thirty-three months after SRT, a limited volume of radiation fibrosis was seen. (E) Forty-three months after SRT, the volume of the fibrosis looked somewhat smaller.

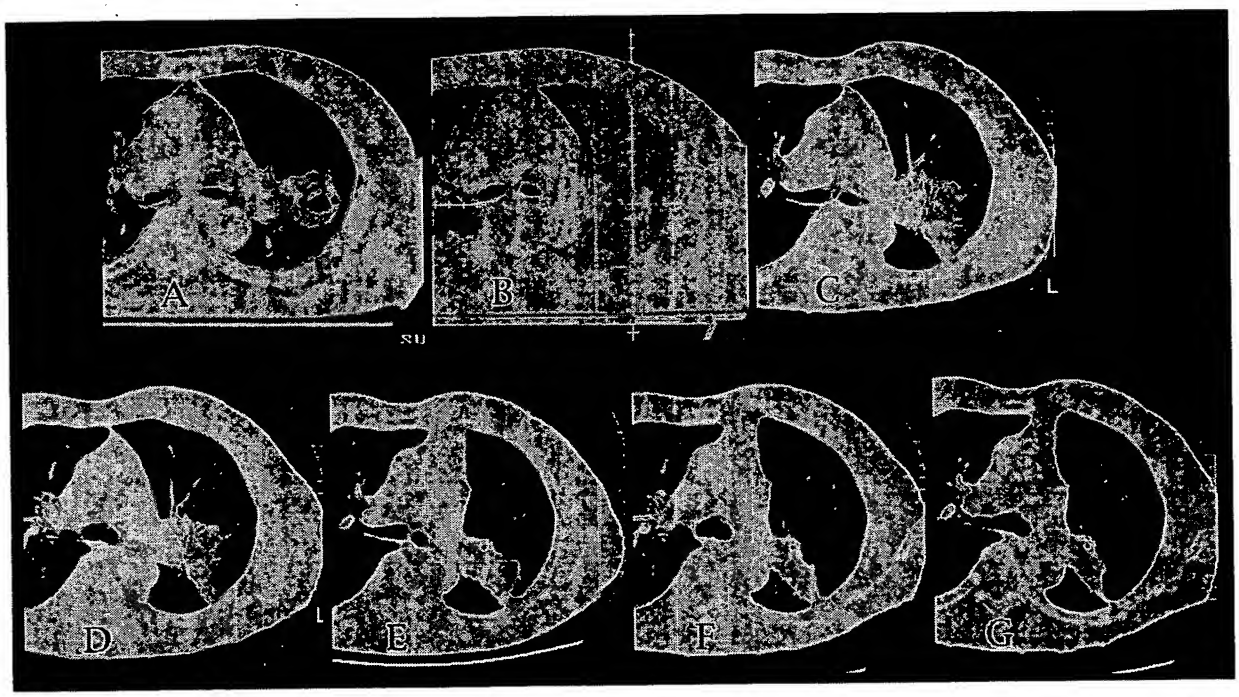

Fig. 2. T2N0M0 squamous cell carcinoma of the lung. (A) A 4.5-cm tumor with the cavity seen on the positioning CT. To reduce the risk of marginal recurrence, conventional RT of 50 Gy in 25 fractions during 5 weeks was initially given. (B) After RT, shrunken tumor (<3 cm) and radiation-induced interstitial changes were seen. SRT of 40 Gy in 8 fractions during 2 weeks was given at the 80% isodose line of 3.5 cm in diameter. (C) Three months after SRT, the tumor was not clear but localized radiation-induced fibrotic changes were apparent. (D) Six months after SRT, the volume of the radiation fibroses was reduced. (E) Nine months after SRT, the volume of the radiation fibroses had reduced further but localized atelectasis was seen. (F) Twenty-five months after SRT, the atelectasis was localized. (G) Fifty-five months after SRT, the volume of the atelectasis was somewhat smaller.

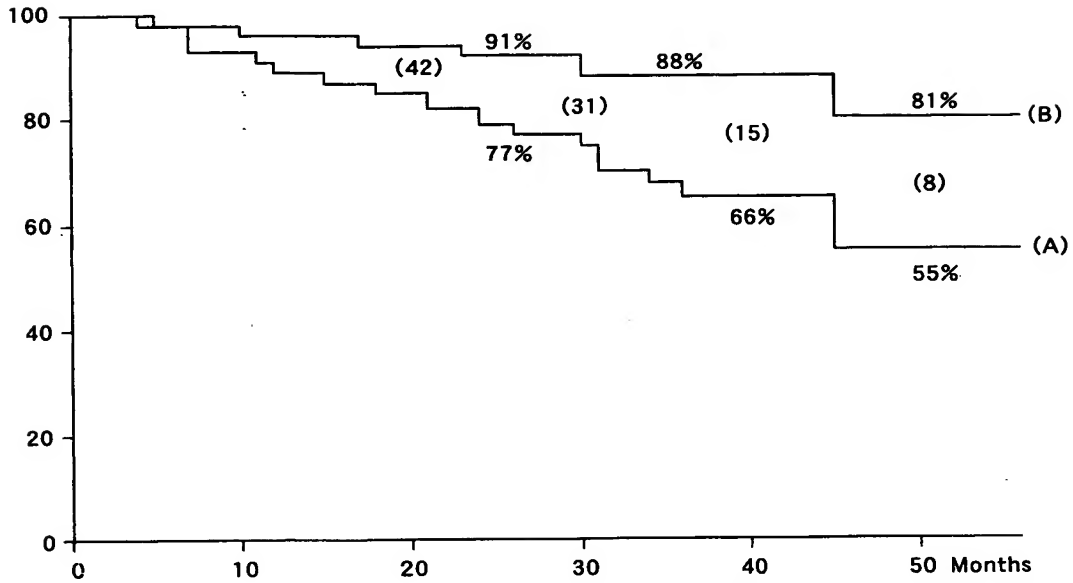

Fig. 3. Actuarial overall (A) and cause-specific (B) survival of all 50 patients. The numbers in parentheses indicate the number of patients at risk beyond those points.

carbon table can move accurately among the linac, CT unit, and X-ray simulator (3, 6).

While lying on the carbon table, the patient practiced shallow respirations with an oxygen mask throughout the daily treatment procedure of positioning and irradiation. An abdominal pressure belt was applied if the respiratory motion needed to be minimized further. The X-ray simulator checked the craniocaudal motion of the lung tumor. Once this motion was <1 cm, serial CT scanning was performed.

The clinical target volume and the center of the target volume were then decided by these CT scan images. The patient was then according to the CT images, aligning the target volume to be irradiated by the linac with multiple noncoplanar arcs. A more detailed account of the method has been previously presented (3, 6). The accuracy of the intrafractional tumor position was studied and reported to always be <1 mm for intracranial and generally <5 mm for extracranial tumors (5, 6).

Between October 1994 and June 1999, 50 patients (35

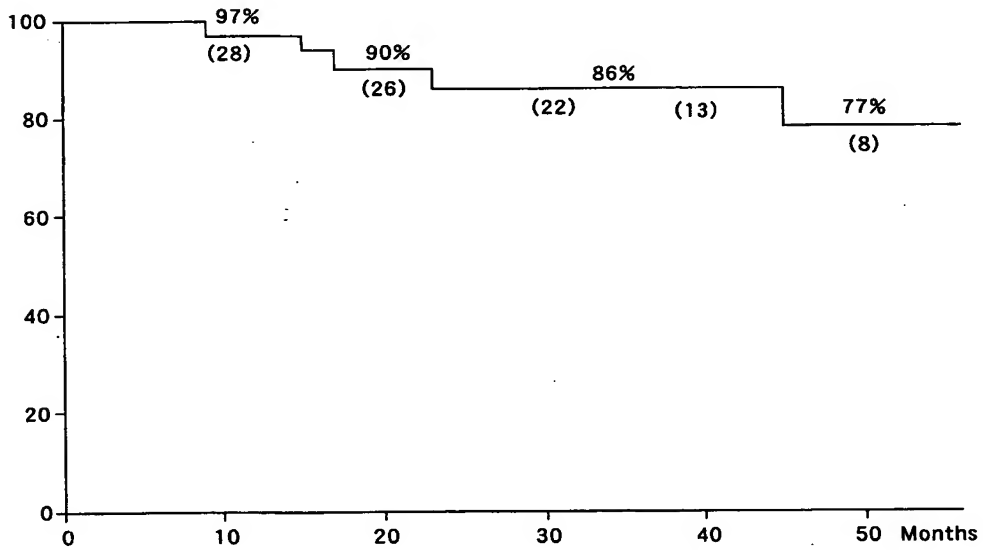

Fig. 4. Actuarial overall survival of the 29 medically operable patients. The numbers in parentheses indicate the number of patients at risk beyond those points.

men and 15 women; age range 54–86 years, median 71) with T1–2N0 M0 NSCLC were treated by CT-guided frameless SRT. All patients had pathologically proven NSCLC (adenocarcinoma, $n = 33$; squamous cell carcinoma, $n = 13$; non–small-cell carcinoma not specified, $n = 4$). Of these, 21 patients were judged to be medically inoperable by the surgeons, including 5 patients who had marked chronic obstructive pulmonary disease and poor respiratory function. The remaining 29 patients were medically operable but refused surgery. The stage was determined in all patients primarily by chest X-rays and chest CT scans; 24 patients had T1N0M0 and 26 T2N0M0 disease. No patients underwent mediastinoscopy. The tumor size was 0.8–5.0 cm (median 3.2) in diameter on the CT scans.

In most patients, SRT was 50–60 Gy in 5–10 fractions within 1–2 weeks. Two T1N0M0 and 16 T2N0M0 patients also received conventional RT (40–60 Gy in 20–33 fractions within 4–6 weeks) before receiving SRT. In 16 of the 18 patients who underwent conventional treatment, the radiation fields covered just the tumor volume with 2-cm margins; only 2 patients received prophylactic nodal irradiation to the hilar and mediastinal regions. In those 18 patients, the total dose delivered by SRT was occasionally reduced to 30–45 Gy in 5–10 fractions. No patients received chemotherapy. Informed consent was obtained from all patients.

The follow-up period for the 33 living patients ranged from 22–66 months (median 36). Chest CT scans were usually performed every 3 months in the initial 2 years and repeated every 4–6 months thereafter. The overall and cause-specific survival rates were calculated by Kaplan–Meier methods (7) from the day of the first visit. Local control was judged when the tumor showed no local progression on follow-up CT scan images.

RESULTS

The CT-guided SRT treatment was safely performed in all 50 patients in this series with no or minimal acute adverse symptoms. With a median follow-up of 36 months, a few subacute or late adverse effects were observed. One patient who received SRT alone had a rib fracture that did not require medical treatment, and 1 patient who received both SRT and conventional RT had a vertebral compression fracture that required temporary medication for pain control. In the patients with a fractured bone, the bony structures were initially adjacent to the lung tumors and were included within the 80% isodose lines of SRT. Nevertheless, these 2 patients were almost symptom free at the last follow-up. The other 6 patients who received both SRT and conventional RT complained of mild and temporary pleural pain, which did not require any medication. On follow-up CT scans, apparent lung fibroses and/or small atelectases were seen in most of the patients who underwent both SRT and conventional RT, although such radiation lung damage was very limited in patients with SRT alone (Figs. 1 and 2).

Table 1. Patterns of failure (final status) ($n = 50$)

Isolated local failure	3*
Isolated nodal failure	0
Isolated distant failure	5†
Nodal and distant failure	2‡

* One alive with disease; 1 dead of disease; 1 dead of other causes (bacterial pneumonia).
† Two alive with disease, 3 dead of disease.
‡ Two dead of disease.

Symptomatic respiratory deteriorations were not observed, even in the 5 patients who had marked chronic obstructive pulmonary disease and poor respiratory function.

Of all 50 patients studied, 30 were alive without any relapses, 3 were alive with disease, 6 had died of disease, and 11 had died intercurrently. The causes of intercurrent death were malignancies other than lung cancer in 3 patients (maxillary cancer, bladder cancer, and leukemia), myocardial infarction in 2, decrepitude in 2, cerebral infarction in 1, bacterial pneumonia in 1, liver failure in 1, and acute abdomen in 1. The 3-year overall and cause-specific survival rate was 66% and 88%, respectively (Fig. 3). Of the 29 medically operable patients, 24 were alive without any relapses, 3 had died of their disease, and 2 had died intercurrently (1 of leukemia and 1 of cerebral infarction). The 3-year overall survival rate was 86% (Fig. 4). The patterns of failure are summarized in Table 1. Local control was achieved on CT scans in 47 (94%) of 50 patients, and isolated regional nodal failures had not been observed at last follow-up.

DISCUSSION

Since the report of the first randomized study by Morrison *et al.*, surgery has been considered a superior treatment to conventional RT for operable NSCLCs (8). Therefore, conventional RT has been used mainly for medically inoperable patients (9). Recently, multiple analyses of the patterns of failure after conventional RT have been performed, and higher radiation doses with smaller radiation volumes have been recommended for the treatment of lung cancers (9–11).

In the current study of SRT, which used very high-dose radiation for the small treatment volume of localized NSCLCs, excellent treatment results were obtained not only for the 21 medically inoperable patients but also for the 29 operable patients. Even though only 2 patients received prophylactic irradiation to the nodal sites, the incidence of regional failure was very low. These findings are compatible with the recent recommendations (9–11). Although the number of patients in this study was only 50 and the median follow-up period was only 36 months, we found that the treatment-related adverse effects were very limited when the patients were treated by SRT alone (Fig. 1).

More recently, several other authors have also reported the results of SRT for lung cancers with or without using an

immobilization body cast and demonstrated very high local control rates and limited adverse effects (12, 13). In view of these SRT results (12, 13) and our current data, it may be appropriate to consider randomized studies to compare surgery with SRT for Stage I NSCLC. At this time, additional studies with longer follow-up periods and an increased number of patients should be warranted to assess this new treatment approach for early-stage lung cancer.

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